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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/775,554	02/09/2004	Meng Yang	312762004400	6701

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MORRISON & FOERSTER LLP
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EXAMINER	
WEHBE, ANNE MARIE SABRINA	
ART UNIT	**PAPER NUMBER**
1633	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/775,554	YANG ET AL.	
	Examiner	Art Unit	
	Anne Marie S. Wehbe	1633	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *11 May 2007*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-3,19 and 20* is/are pending in the application.

4a) Of the above claim(s) *19 and 20* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-3* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Applicant's amendment and response received on 5/11/07 has been entered. Claims 4-18 have been canceled. Claims 1-3 and 19-20 are pending in the instant application. This application contains claims 19-20 drawn to an invention nonelected without traverse. A complete reply to the final rejection must include cancellation of nonelected claims or other appropriate action (37 CFR 1.144) See MPEP § 821.01. Claims 1-3 are currently under examination in the instant application. An action on the merits follows.

Those sections of Title 35, US code, not included in this action can be found in the previous office action.

Claim Rejections - 35 USC § 112

The rejection of claims 1-3 under 35 U.S.C. 112, second paragraph, for indefiniteness are withdrawn in view of the amendments to claims 1 and 3.

Claim Rejections - 35 USC § 102

The rejection of claims 1-3 under 35 U.S.C. 102(a) as being anticipated by WO 02/28188 A1 (4/1/02), hereafter referred to as Kern, is maintained. Applicant's amendments and arguments have been fully considered but have not been found persuasive in overcoming the rejection for reasons of record as discussed in detail below.

The claims as amended are now product by process claims as the claim amendments introduce a process of breeding to obtain the claimed immunocompromised transgenic rodent. The applicant argues that Kern is a prophetic disclosure and that the process as now claimed to make the mice through breeding is not taught by Kern. The applicant further argues that as the genetic makeup of the mice disclosed by Kern is difficult to determine, it must therefore be different from the genetic makeup of the mice as now claimed. In particular, the applicant argues that the "fourth" cross now recited in the claims is an innovation that results in maintenance of immunodeficiency. Based on these arguments, the applicant concludes that Kern cannot anticipate or inherently disclose the specific rodent now claimed. It is also noted that the applicant cites from various published cases including *In re Robertson*, *In re Oelrich*, *Glaxo Inc. v. Novopharm Ltd.*, *Ex parte Phillips*, *In re Best*, and *Ex parte Gray*, in support of their position that the rejection must show that the claimed rodents must inevitably result from the procedure taught by Kern.

In response, it is first noted that the claims as amended are now product by process claims. The applicant is reminded that "[E]ven though product-by-process claims are limited by and defined by the process, determination of patentability is based on the product itself. The patentability of a product does not depend on its method of production. If the product in the product-by-process claim is the same as or obvious from a product of the prior art, the claim is unpatentable even though the prior product was made by a different process." *In re Thorpe*, 777 F.2d 695, 698, 227 USPQ 964, 966 (Fed. Cir. 1985) (citations omitted). In the instant case, the rejection of record set forth that Kern teaches a transgenic immunodeficient organism which exhibits a detectable trait such as the expression of a detectable marker (Kern, page 4). Kern

specifically teaches that the organism is a transgenic mouse, and more specifically the offspring of a nu/nu mouse, which expresses the detectable marker green fluorescent protein (Kern, page 4, and page 23, claims 18-24). Kern further teaches methods of making the mouse by stably integrating the detectable gene into the chromosome of a mouse embryonic stem cell and using the embryonic cell to develop strains of homozygous mice having two copies of the integrated construct in every cell, and then breeding the mice with nu/nu mice to produce mice that are homozygous for the transgene and homozygous for immunodeficiency (Kern, pages 10-11). Kern further teaches the constitutive expression of green fluorescent protein in the nu/nu mice (Kern, page 13). Note in particular that Kern et al. teaches breeding the mouse transgenic for the selectable trait, such as constitutive GFP expression, to heterozygosity or homozygosity, where the transgene is integrated into the chromosomes of every cell in the mouse, and then cross-breeding that strain to a nu/nu mouse strain to create a homozygous GFP+/GFP+:nu/nu mouse or a heterozygous GFP+/-:nu/nu mouse (Kern, pages 10-11, bridging paragraph). The nu/nu mice are genetically immunodeficient as they lack essential immune effector cells. The GFP protein is an immunofluorescent protein that has no immunological function and cannot reverse or compensate for the severe genetic immunodeficiency caused by the nu/nu genotype. The previous office action therefore indicated that a GFP+/GFP+: nu/nu mouse would clearly maintain its immunodeficiency as it is homozygous for the nu/nu mutations. Applicant's argument that the additional breeding step included in the claims, referred to as the "fourth" cross, would clearly affect the genetic makeup of the mouse is not agreed as the specification does not teach that such mice possess any specific structural properties that set them apart from mice produced from fewer breeding crosses or from additional breeding crosses. Note that the

claims as amended further recite that following the "fourth" cross, those mice can be bred again, such that the claimed mice are not in fact limited to the progeny of the "fourth" cross. As such, the structure of the mice taught by Kern et al. appears to be identical to that claimed, regardless of whether additional crosses were made or not, as long as the mice express GFP in very tissue except erythrocytes and hair and are immunocompromised or nu/nu. It is also noted that neither the specification nor the applicant's response provides any evidence that the "fourth" cross somehow results in a structural change that affects maintenance of immunodeficiency as compared to mice produced from the "third" cross or from fifth or sixth crosses. Therefore, the mice taught by Kern et al., made by a similar though not identical method, appear to be identical in structure to the claimed mice.

In addition, regarding applicant's comments that as the Kern specification is prophetic the case law cited in the previous office action, *Ex parte Phillips*, *In re Best*, and *Ex parte Gray*, is not on point because the Kern product was not made, the applicant is reminded that case law states that anticipation does not require the actual creation or reduction to practice of the prior art subject matter; anticipation requires only an enabling disclosure. *In re Donohue*, 766 F.2d 531, 533 [226 USPQ 619] (Fed. Cir. 1985). A reference may enable one of skill in the art to make and use a compound even if the author or inventor did not actually make or reduce to practice that subject matter. *Bristol-Myers*, 246 F.3d at 1379; see also *In re Donohue*, 766 F.2d at 533. Kern clearly meets this burden as the Kern reference provides substantial guidance for making transgenic mice and breeding them to nude mice. In addition, none of the cited case law states that inherency may only be established if the reference discloses having made the disclosed product. Thus, there is no requirement in the cited case law stating that the prior art reference

must provide a specific example wherein the product disclosed was actually made in order to demonstrate anticipation or inherency.

Further, it is noted that the discussion of "inherency" in the rejection of record was in reference to the expression pattern of the GFP in the GFP/nude mouse, and not the maintenance of immunodeficiency. Kern clearly teaches GFP+/GFP+:nu/nu mice. As discussed above, the homozygous nu/nu genotype of these transgenic mice renders them immunocompromised. The previous office action stated that while Kern doesn't teach that the resulting nu/nu GFP mouse expresses GFP in "essentially all tissues", the limitation previously recited in the claims, Kern does teach that the transgene is present in all cells of the mouse and that the expression is constitutive due to the use of a constitutive promoter such that global expression would be an inherent characteristic of the mouse. The claims as amended now recite that GFP is expressed in all tissues except erythrocytes and hair. Again, as Kern teaches that the GFP transgene operatively linked to a constitutive promoter is present in the genome of every cell in the transgenic mouse, global GFP expression would be an inherent characteristic of the mice as constitutive promoters are not cell specific and are capable of expressing an operably linked coding sequence in all cells possessing a genome comprising the transgene. Note as well that as erythrocytes do not have nuclei, i.e. no chromosomes, no expression in erythrocytes would be possible. Likewise, hair is the product of dead cells that have lost their nuclei and is composed primarily of keratin and melanin. Hair cannot "express" a fluorescent protein as it does not contain genetic material capable of being expressed. Thus, the mice taught by Kern would inherently express GFP in all tissues except hair and erythrocytes. Once a reference teaching a product appearing to be substantially identical is made the basis of a rejection, and the examiner

presents evidence or reasoning tending to show inherency, the burden shifts to the applicant to show an unobvious difference. MPEP 2112. V, emphasis added. Further, MPEP 2112 states that "[T]he PTO can require an applicant to prove that the prior art products do not necessarily or inherently possess the characteristics of his [or her] claimed product. Whether the rejection is based on 'inherency' under **35 U.S.C. 102**, on '*prima facie* obviousness' under **35 U.S.C. 103**, jointly or alternatively, the burden of proof is the same...[footnote omitted]." The burden of proof is similar to that required with respect to product-by-process claims. *In re Fitzgerald,* 619 F.2d 67, 70, 205 USPQ 594, 596 (CCPA 1980) (quoting *In re Best,* 562 F.2d 1252, 1255, 195 USPQ 430, 433-34 (CCPA 1977)). Finally, note that there is no "missing descriptive matter" in the Kern reference except for specific disclosure of global GFP expression. However, Kern teaches a GFP+/GFP+:nu/nu mouse where GFP is under the control of a constitutive promoter and is present in all cells possessing a genome. Based on the properties of constitutive promoters and the nature of erythrocytes and hair discussed in detail above, the Kern mice inherently express GFP in all tissues except hair and erythrocytes. As such, applicant's arguments and claim amendments are not found persuasive in overcoming the rejection of record.

No claims are allowed.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO

MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication from the examiner should be directed to Anne Marie S. Wehbé, Ph.D., whose telephone number is (571) 272-0737. If the examiner is not available, the examiner's supervisor, Joseph Woitach, can be reached at (571) 272-0739. For all official communications, **the new technology center fax number is (571) 273-8300**. Please note that all official communications and responses sent by fax must be directed to the technology center fax number. For informal, non-official communications only, the examiner's direct fax number is (571) 273-0737. For any inquiry of a general nature, please call (571) 272-0547.

The applicant can also consult the USPTO's Patent Application Information Retrieval system (PAIR) on the internet for patent application status and history information, and for electronic images of applications. For questions or problems related to PAIR, please call the USPTO Patent Electronic Business Center (Patent EBC) toll free at 1-866-217-9197. Representatives are available daily from 6am to midnight (EST). When calling please have your application serial number or patent number available. For all other customer support, please call the USPTO call center (UCC) at 1-800-786-9199.

Dr. A.M.S. Wehbé

/Anne Marie S. Wehbé/
Primary Examiner, A.U. 1633